News and Resources from the National Institutes of Health

Diabetes Dateline

National Diabetes Information Clearinghouse

Spring 2006

Tight Control of Blood Glucose Cuts Heart Disease, Stroke in Type 1 Diabetes

Results Confirm Long-Term Benefits of Aggressive Treatment

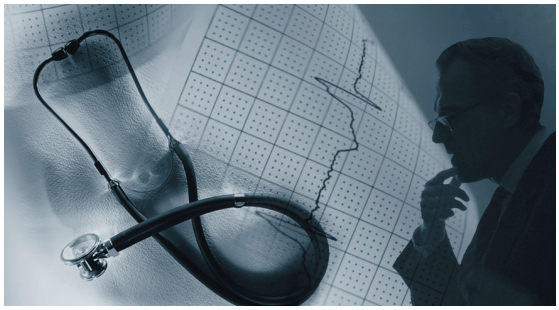
People with type 1 diabetes who tightly control their blood glucose levels are less likely to develop cardiovascular disease when compared with those who do not keep blood glucose levels as low, according to a long-term look at more than 1,300 patients who took part in the Diabetes Control and Complications Trial (DCCT), a large clinical study that began more than 2 decades ago. The findings were published in the December 22, 2005, issue of the *New England Journal of Medicine*.

While researchers have long known about a link between diabetes and heart attacks, stroke, and angina, the study results provide the most solid evidence that careful glucose control lowers the risk of cardiovascular events.

Strong Results

"There was absolutely no previous clinical trial evidence that lowering blood glucose in type 1 or type 2 diabetes would reduce cardiovascular disease complications," said Saul Genuth, M.D., chairman of the study and professor of medicine at Case Western University. "We were somewhat surprised at the strength of the observation. We found, in raw terms, practically a 50 percent reduction in nearly every cardiovascular outcome we measured."

The DCCT enrolled 1,441 patients between the ages of 13 and 39, following them through an average treatment of more than 6 years. Patients in the intensive treatment group measured their blood sugar at least four times a day and administered insulin three or more times a day.



Patients in the conventional treatment group received one or two doses of insulin a day. In 1993, researchers announced the DCCT's first major finding: intensive glucose control greatly lowers the eye, nerve, and kidney damage of type 1 diabetes.

Lasting Effects

As researchers continued following the DCCT participants over the years, they saw that the blood glucose levels of the intensively treated group gradually rose. In contrast, the glucose levels of those originally assigned to conventional glucose control had dropped, since they were taught how to strictly control their glucose levels.

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Saul Genuth, M.D.
DCCT chairman and professor of medicine at Case Western University

Still, the time spent in intensive treatment has had lasting positive effects, a phenomenon known as "metabolic memory."

Among those intensively treated during the DCCT, 4 percent suffered a cardiovascular disease event, such as a heart attack or angioplasty procedure, compared with 7 percent of those in the conventionally treated group. The average age of the participants was 45 years.

Implications for Type 2 Diabetes

The results are specific to the type 1 population, said Catherine Cowie, Ph.D., who oversees the study for the National Institute of Diabetes and Digestive and Kidney Diseases, which funds the research. "The findings reinforce the current standards of clinical care," she said. "Extending the conclusions to people with type 2 diabetes is more difficult."

"We can probably extrapolate to type 2 diabetes, but that is challenging because it is an older population that is complicated by obesity and high blood pressure," Cowie said. That question is being addressed by the Action to Control Cardiovascular Risk in Diabetes study.

The study results reinforce the earlier DCCT findings, which show that tight glucose control leads to lower rates of neuropathy, nephropathy, and retinopathy. Now, Genuth said, investigators will look at whether the years of intensive treatment will translate into lower rates of vision loss, kidney failure, and, eventually, improved survival. ■

Diabetes Dateline Gets a New Look, Will Appear More Often

Longtime readers may notice some changes both in look and content in this issue of *Diabetes Dateline*. We have redesigned the publication, putting fresh news from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in a new package.

Readers will be seeing the publication more often. Traditionally published twice a year, we now plan to produce the newsletter quarterly.

The front page format has been redesigned to highlight each issue's main topic. The top of each page highlights the featured topic.

Diabetes Dateline will continue its focus on bringing the latest in NIDDK news and updates from the National Diabetes Information Clearinghouse, and we will also search for stories about the most interesting people and projects at the agency.

Our effort to produce the highest quality, most interesting publication requires the help of our readers. If you know of stories *Diabetes Dateline* should be chasing or profiles that it should be running, please contact the newsletter staff at 703–902–1302. ■

Diabetes
Dateline

Diabetes Dateline is published four times a year by the National Diabetes Information Clearinghouse (NDIC). The newsletter features news about diabetes special events, patient and professional meetings, and new publications available from the NDIC and other related organizations.

Subscriptions are free but available only to health professionals. Send subscription inquiries to: National Diabetes Information Clearinghouse, 1 Information Way, Bethesda, MD 20892–3560. This publication is also available online at *www.diabetes.niddk.nih.gov/about/newsletter.htm*.

Registry Offers Broad Picture of Islet Transplant Safety, Effectiveness

The Collaborative Islet Transplant Registry (CITR) has released its second annual report, offering researchers and doctors an in-depth look the safety and efficacy of 266 islet infusions in 138 patients. The procedures were performed at 19 different medical centers around the globe.

The CITR, which opened in the fall of 2002, was designed to combine data from a number of different centers. Because islet transplantation remains a cutting-edge and infrequently performed procedure for patients with type 1 diabetes who have hypoglycemia or require a kidney transplant, no single institution can hold its experience up as being representative of the field.

"The registry is still quite young, but it's doing a very good job of providing critical information about the results of islet transplantation," said Michael Appel, Ph.D., who oversees the project for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). "As the registry matures, researchers will be able to use the data to identify factors that increase risk and those that promote success. This information will help centers refine their protocols based on objective information."

Smaller Numbers, Larger Challenges

Drug trials often include thousands of patients, allowing researchers to quantify what kinds of side effects can be expected. Developing the same profile with the small number of islet transplantations is difficult, but the pooling of data in the registry will give researchers a better idea of adverse event frequency.

The CITR audits and compiles data from each center, offering a fuller picture of the procedure's successes and limitations. Of the 138 patients tracked thus far, 68 percent were insulin-independent 6 months after their last islet transplant, with 58 percent not injecting insulin a year after the final procedure. Those who still required insulin used less of the drug than before the procedure.

Little Hypoglycemia

Only 2.5 percent of patients who received an injection of islets reported problems with hypoglycemia in the month following the injection, and only 2 percent reported problems beyond a month.

Also important is the safety data collected, because a single center cannot usually evaluate enough adverse events to determine the real side effect profile of the treatment. The collected data did not reveal any surprises. "We have a handle on the safety profile. There weren't any things that were unexpected," said Appel.

The number of patients in the registry should continue to climb as more centers come on board and more procedures are performed. The number of patients for whom data will be available will double in the next year, according to Thomas Eggerman M.D., Ph.D., the director of the NIDDK's islet transplantation program.

Data from the CITR is available on the registry's website at *www.citregistry.org*. ■

Copies of the CITR annual report can be ordered from the National Diabetes Information Clearinghouse's website at *www.catalog.niddk.nih.gov* (publication number DM-245).

New Centers Funded

In an effort to build understanding about how islet transplantation works and how to improve the procedure, the National Institutes of Health is spending $75 million over 5 years to fund islet transplant studies at five facilities.

By pooling their resources, researchers will be better able to probe new methods, said Thomas Eggerman, M.D., Ph.D., who manages the consortium. Seven protocols are being developed, and the trials are planned for 2006.

In addition, the five centers—the University of Miami, the University of Minnesota, the University of Pennsylvania, the University of Alberta, and Uppsala University in Sweden—and the University of Iowa-based data coordinating center can work together to build the kind of large multi-center trials needed to obtain regulatory approval to conduct the clinical studies.

Seven Initiatives Seek to Bridge Basic, Clinical Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is pushing to improve the ability of researchers to turn breakthroughs in basic science into new patient treatments and tests, focusing its attention on several initiatives designed to promote this translational research.

The effort to boost translational research follows a high-profile 2003 call to action by participants in the Institute of Medicine's Clinical Research Roundtable. Those researchers, writing in the *Journal of the American Medical Association,* said they were worried that scientific breakthroughs "are failing to be translated efficiently into tangible human benefit."

Part of NIH Roadmap

The National Institutes of Health (NIH) has made promotion of translational research a centerpiece of its "Roadmap for Medical Research in the 21st Century," and the NIDDK will concentrate its resources in seven areas, including better imaging technologies, better animal models, and a more vigorous search for drugs to treat diseases caused by misformed proteins.

"Concrete initiatives are coming out of this," said Allen Spiegel, M.D., former director of the NIDDK, who said the effort is designed to help fill "valleys of support" in the research spectrum.

Spiegel acknowledged that the move toward more robust translational research at the NIH will require partnerships with industry, such as pharmaceutical companies, which often foots the bill for later-stage research. "If we are to be successful in translational research, we will have to be extremely thoughtful in how we deal with industry." ■

The Seven Translational Areas

- **Biomarkers:** The NIDDK is encouraging researchers to examine new ways to assess disease progression and treatment effects through the use of new tests using blood, tissue, and other samples.
- **Imaging of Solid Abdominal Organs and the Urinary Tract:** Doctors are often frustrated by the lack of reliable noninvasive ways of monitoring digestive, kidney, and urinary health, prompting an effort to find better imaging technology and techniques that will allow physicians a more precise understanding of these diseases.
- **Animal Models:** The NIDDK is pushing researchers to work on finding new or improved animal models in an effort to improve the safety and efficacy testing of new therapies that must be done before a treatment is offered to humans.
- **Angiogenesis and Diabetes:** Control of angiogenesis—the process by which the body creates new blood vessels—could lead to better understanding of several complications of diabetes, such as wound healing and nerve damage, and research into this process may improve the outcomes of islet transplant in patients with type 1 diabetes.
- **Preventing Oxidative Stress:** Hyperglycemia, or high blood glucose, often causes a buildup of damaging oxygen molecules in a part of the cell called the mitochondria. The NIDDK is encouraging researchers to find new ways to halt that process, and thereby lessen complications from diabetes.
- **New Therapies Targeting Proteins:** Errors in the way proteins are made and used in the body are responsible for a range of diseases; this effort seeks to find molecules capable of stopping those defects.
- **RNA Interference:** The NIH would like researchers to realize the promise of therapies that interfere with messenger RNA molecules responsible for disease processes, an early-stage research effort that has generated many unresolved issues.

NIDDK Welcomes Five New Members to Advisory Council

Five new members have been named to the Advisory Council of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The body serves both to guide the NIDDK's discussion of broad science policy issues and to provide second-level review of funding requests. The new members, who will serve until 2009, are:

David M. Klurfeld, Ph.D.: Klurfeld serves the U.S. Department of Agriculture as a national program leader in human nutrition in the Agricultural Research Service, where he oversees research designed to define the role of food and its constituents in optimizing health. Klurfeld will join the Digestive Diseases and Nutrition Subcommittee.

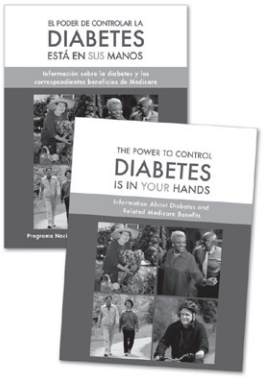
From left to right: David H. Perlmutter, M.D., David M. Klurfeld, Ph.D., Juanita Lynne Merchant, M.D., Ph.D., Mitchell A. Lazar, M.D., Ph.D., Griffin P. Rodgers, M.D., Acting Director, NIDDK, and Margery Deutz Perry. Photo credit: NIDDK.

Mitchell A. Lazar, M.D., Ph.D.: Lazar is a Sylvan H. Eisnman Professor of Medicine and Genetics and chief of the division of endocrinology, diabetes, and metabolism at the University of Pennsylvania School of Medicine in Philadelphia, and he directs the Institute for Diabetes, Obesity, and Metabolism at the Hospital of the University of Pennsylvania in Philadelphia. Lazar joins the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee.

Juanita Lynne Merchant, M.D., Ph.D.: A professor of internal medicine and molecular and integrative physiology at the University of Michigan, Merchant studies how bacterial colonization in the gastrointestinal tract can lead to ulcers and cancer. She joins the Digestive Diseases and Nutrition Subcommittee.

David H. Perlmutter, M.D.: Perlmutter is the Vira I. Heinz Professor and Chair of Pediatrics and a professor of cell biology and physiology at the University of Pittsburgh School of Medicine, the scientific director of the John G. Rangos Sr. Research Center, and physician-in-chief at Children's Hospital of Pittsburgh. Perlmutter studies liver disease and will join the Digestive Diseases and Nutrition Subcommittee.

Margery Deutz Perry: The past chair of research at the Juvenile Diabetes Research Foundation (JDRF) International, Perry oversaw both the development and implementation of the JDRF's research goals and priorities. In addition, she supervised and approved all aspects of the JDRF's research programs. Perry joins the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee. ■



NDEP Revises *Power to Control Diabetes* Campaign

The National Diabetes Education Program (NDEP) has revised its popular *The Power to Control Diabetes is in Your Hands* campaign. The effort is aimed at older Americans and their loved ones and is intended to give patients with diabetes and their families the information they need to manage the disease.

The Power to Control brochure is available in both English and Spanish and offers suggestions on managing blood glucose, blood pressure, and cholesterol levels. In addition, the publication offers advice on medication usage, lifestyle choices, and ways to access Medicare benefits.

Campaign materials are available via the NDEP website at *www.ndep.nih.gov*. ■

New From NDIC:

Diagnosis of Diabetes

Patients seeking basic information about the diagnosis of diabetes, the sixth-leading cause of death in the United States, now have an additional resource in the National Diabetes Information Clearinghouse's *Diagnosis of Diabetes*.

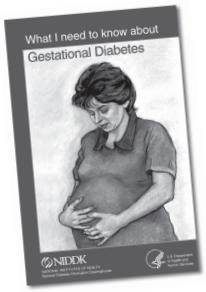
This booklet discusses the methods of testing for diabetes and pre-diabetes and explains the distinction between normal plasma glucose levels and levels that signify diabetes and pre-diabetes, which is indicated by impaired glucose tolerance or impaired fasting glucose. The two different tests can point to the same problem: pre-diabetes.

The publication explains the risk factors for the disease, including age and ethnic background, encouraging those at risk to be tested. It also includes body mass index tables so patients can determine if they are overweight or obese—significant risk factors for the development of type 2 diabetes.

Finally, *Diagnosis of Diabetes* includes information on how to keep diabetes at bay for those at high risk of developing the disease, drawing upon the lessons of the Diabetes Prevention Program Trial, which found that people with pre-diabetes were less likely to develop diabetes after implementing lifestyle changes.

To order, please call 1–800–860–8747 or visit *www.diabetes.niddk.nih.gov*.

What I need to know about Gestational Diabetes



A new publication aimed at improving care for the hundreds of thousands of women a year who develop gestational diabetes during their pregnancy is now available from the National Diabetes Information Clearinghouse.

The 20-page booklet, *What I need to know about Gestational Diabetes*, describes the condition and its causes, and it offers pregnant women and those at risk for the condition a roadmap to the diagnosis and treatment of gestational diabetes. Written in an easy-to-read style at a fourth- to sixth-grade reading level, the booklet also features colorful, multi-ethnic illustrations.

The publication details the risks that come when the condition is untreated or undertreated, including overweight babies and breathing difficulties in newborns. And because women with gestational diabetes are at higher risk for type 2 diabetes later in life, the publication tracks the postpartum steps mothers should take to help ensure that they remain healthy after giving birth.

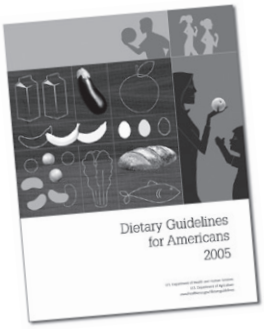
What I need to know about Physical Activity and Diabetes

The National Diabetes Information Clearinghouse has published a new booklet designed to help people with diabetes manage their blood glucose and cut their risk of long-term complications, such as heart disease and stroke, through exercise.

The publication, *What I need to know about Physical Activity and Diabetes*, walks readers through four types of activity shown to help patients stay healthy. Patients are encouraged to be extra active every day, do aerobic exercise, strength train with weights or elastic bands, and stretch.

The 16-page booklet, written at a fourth- to sixth-grade reading level, also details the unique risks that people with diabetes may face, such as unnoticed blisters and the possibility of hypoglycemia, also called low blood glucose.

What I need to know about Physical Activity and Diabetes also emphasizes the preventative benefits of exercise for patients with impaired glucose tolerance, citing the results of the Diabetes Prevention Program Trial. That 3,234-patient clinical study found that patients at risk for diabetes cut the odds of developing the disease by more than 50 percent after losing weight by cutting calories and fat and exercising regularly. ■



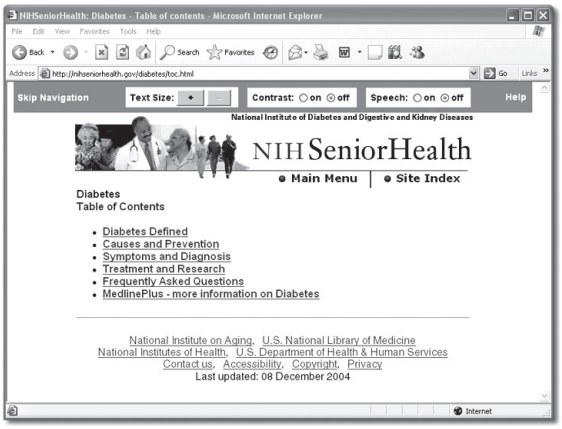
New Dietary Guidelines Designed to Cut Obesity, Diabetes, Heart Ailments

The U.S. Government published its latest set of dietary guidelines with a more pointed emphasis on calorie intake and physical exercise as part of an effort to help Americans stave off chronic diseases such as diabetes and heart disease.

Dietary Guidelines for Americans 2005 offers consumers more specific advice with regard to foods, setting recommendations for the amount of saturated fats consumed, and keeping trans fat consumption to a minimum. In addition, the report suggests 60 minutes of physical activity a day to maintain weight, up from 30 minutes in the 2000 guidelines.

New Online Diabetes Resource for Seniors Launched

The National Institute of Diabetes and Digestive and Kidney Diseases and the National Institute on Aging have added a diabetes page to the popular National Institutes of Health Senior Health website. The diabetes page is located at *nihseniorhealth.gov/diabetes/toc.html* and features information about the disease and its causes, symptoms, treatments, and research. In addition, the site gives visitors access to an easy-to-read list of frequently asked questions and offers a link to the Government's more extensive MedlinePlus page.



Researchers Explore Lifecycle of Insulin-Producing Cells

Scientists from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) have successfully taken insulin-producing cells from the pancreas of a cadaver and induced them to revert back to easy-to-reproduce precursor cells.

The early-stage research was published in the December 2004 issue of the journal *Science*. The findings are not expected to have immediate applications in treatment, according to Marvin Gershengorn, M.D., scientific director of the NIDDK's division of Intramural Research and the lead author of the study, but the findings will help researchers better understand the lifecycle of the cells in the pancreas.

Pancreatic cells called beta cells pump out insulin as part of spherical clusters, or islets, but little is known about the process by which beta cells are regenerated. A better understanding of that process could someday help boost the number of islets available for islet transplantation, an experimental treatment for type 1 diabetes.

Fast-Food Aficionados Gain Weight, Increase Diabetes Risk, Study Says

A 15-year examination of the eating habits of young adults found that those who ate at fast-food restaurants more than two times a week gained 10 pounds more than their peers who dined at such establishments less than once a week, according to a study funded by the National Heart, Lung, and Blood Institute and published in the journal *The Lancet*.

In addition, the frequent fast-food consumers had twice the risk of insulin resistance, a risk factor for type 2 diabetes. The researchers emphasized that despite efforts to include healthier offerings, the restaurants still primarily serve foods that are high in fat and sugar and low in fiber and nutrients. ■

Spiegel to Leave Post as NIDDK Director to Become Dean at Einstein

Allen Spiegel, M.D., has stepped down as director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) after a career at the National Institutes of Health (NIH) that has spanned more than 3 decades, including more than 6 years at the helm of the NIDDK.

"Not only has he been a leader at NIDDK, he's been a leader across NIH."

Elias Zerhouni, M.D.
Director of the National Institutes of Health

Effective June 1, Spiegel will take over the reins at Albert Einstein College of Medicine in the Bronx as dean of the school.

"For nearly 33 years, aside from my family, the NIH has been the most important thing in my life. This has been an extraordinary experience for me, and a privilege," he said. "But I really feel that change is appropriate. It is time for a new and different challenge."

Griffin Rodgers, M.D., the NIDDK's deputy director, is now the NIDDK's acting director.

Spiegel's impact reached beyond the NIDDK. He tackled cross-Institute challenges at the NIH and earned the respect of other directors and the confidence of Elias Zerhouni, M.D., the director of the NIH.

"All of us here at NIH are sad, and we'll miss him. Not only has he been a leader at NIDDK, he's been a leader across NIH," said Zerhouni, who lauded Spiegel's contributions to the NIH during the NIDDK Advisory Council Meeting in February. "Whatever Allen does, he does extremely well and with grace and insight. Allen sees the weakness of an argument with the mind of a Supreme Court lawyer."

After completing his medical residency at Massachusetts General Hospital in 1973, Spiegel came to the NIDDK, quickly rising through the ranks to become a senior investigator, then chief of the Molecular Pathophysiology Section, and then chief of the Metabolic Diseases Branch. He served as the NIDDK's scientific director for 9 years before assuming the role of the NIDDK director in 1999. ■

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